directed to a non-elected invention. Accordingly, Claims 1, 2, 6-8, 11, 12 and 14 remain pending in the present application.

2. Objections to the Claim

Applicant has amended Claim 1 pursuant to the Examiner's objections. Applicant appreciates the Examiner pointing out that "blood stream" is one word and that an article needs to precede the word. Accordingly, Applicant has made the required correction. Applicant respectfully states the above-described amendment does not introduce new matter. Accordingly, the objections to the claim is obviated.

3. Response to Rejection of Claims 1, 2, 6-8, 11, 12 and 14 based upon 35 U.S.C. §112, first paragraph

Claims 1, 2, 6-8, 11, 12 and 14, the remaining pending claims, stand rejected under 35 U.S.C. §112, first paragraph.

The first time the Examiner raised this type of rejection occurred in the first Office Action dated October 22, 1999 (Paper No. 3). The rejection was traversed by Applicant's response to the Office Action dated April 20, 2000 (Paper No. 6). The Examiner withdrew the rejection in the second Office Action dated July 17, 2000 (Paper No. 7) stating that Applicant made the statement in prosecution of the claims that "the claimed invention is not intended to be used for gene therapy". Applicant was particularly concerned with prosecution history estoppel and therefore respectfully informed the Examiner that Applicant did not make any such disclaimer. Applicant's response to the rejection was that the claimed invention was directed to the delivery of a protein to the blood in vivo, which the Examiner had previously noted was enabled by the Specification.

The second time that the Examiner raised this rejection was in the third Office Action dated October 25, 2001 (Paper No. 14). This rejection was maintained by the Examiner in the present fourth Office Action Final dated July 15, 2002.

The Examiner alleges that the specification does not enable one of ordinary skill in the art to use the invention commensurate in scope with the claims. The Examiner supports his rejection by finding that the claimed invention encompasses gene therapy which is not enabled by the present specification and would require undue experimentation as further specified in Paper 14. The Examiner uses the factors enunciated in In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988) to determine that the specification's disclosure is insufficient such that undue experimentation would be required to practice gene therapy. This rejection is respectively traversed.

The dispositive issue in the present application is "What is the claimed invention?" Applicant maintains that as defined, the present claimed invention is to a method for producing and delivering protein in vivo. More specifically, the method comprises inserting into a vector a promoter which is active only in progenitor cells of red blood cells, and a gene encoding a protein which is non-native to red blood cells, wherein said promoter and said gene are operably linked; collecting an amount of progenitor cells of red blood cells from a mammal; transfecting said progenitor cells of red blood cells in vitro with said vector containing said promoter and said gene; introducing the transfected progenitor cells of red blood cells back to said mammal, wherein the transfected progenitor cells of red blood cells produce altered red blood cells containing said protein which is non-native to red blood cells in vivo in said mammal, and wherein said protein which is non-native to red blood cells is contained only in said altered red blood cells, and thereafter said protein which is non-native to red blood cells is released into a bloodstream of said mammal through rupture of said altered red blood cells. From the bloodstream, the protein can be delivered to the functional site or organs and tissues by the circulating blood system.

However, Applicant's claimed invention is not a mechanism of protein intake by a specific cell. Furthermore, although the present invention can be used for disease treatment as apparent to one skilled in the art, Applicant claimed invention as defined by the claims is not, nor intended to be, a specific gene therapy protocol.

Whether a claim is enabled under 35 U.S.C. 112, paragraph 1 is a question of law, although based upon underlying factual findings. See PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ 2d 1618, 1623 (Fed. Cir. 1996); In re Goodman, 11 F.3d 1046, 1049-50, 29 USPQ 2d 2010, 2013 (Fed. Cir. 1993).

The first paragraph of 35 U.S.C. 112 states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The present rejection is based upon the Examiner's definition of what subject matter is encompassed by the claims and not on the Specification and plain meaning of the claim words. The Examiner has attempted to expand the claims to encompass gene therapy merely because it is mentioned in the Specification. However as held in Raytheon Co. v. Roper Corp, 724 F.2d 951, 957, 220 USPQ 592, 597 (Fed. Cir. 1983), *Cert. Denied,* 469 U.S. 835 (1984), "That claims are interpreted in light of the specification does not mean that everything in the specification must be read into the claims."

The Examiner has failed to point out any particular claim elements, which are broader than a method of producing a protein only in the progenitor cells of red blood cells, and delivering produced protein into bloodstream by rupture of the red blood cells such that the claim elements are not enabled. Enzo Biochem Inc. v. Calgene Inc., 188 F.3d 1362, 1371, 52 USPQ2d 1129 (Fed. Cir. 1999).

In addition, the Examiner has failed to point out any inconsistency in the plain meaning of the claim terms to indicate that the claim terms are broader than a method of producing a protein only in the progenitor cells of red blood cells, and delivering produced protein into blood stream by rupture of the red blood cells such that the claim terms are not enabled. National Recovery Techs., Inc. v. Magnetic Separation Sys., Inc., 166 F.3d 1190, 1194, 49 USPQ2d 1671, 1674 (Fed. Cir. 1999).

The subjective Examiner's view is not consistent with objective views that:

1) Gene therapy is a separate invention from Applicant's claimed mechanism for

delivery of a protein. More specifically, a gene therapy can use a different protein delivery mechanism other than Applicant's claimed invention of a specific mechanism for the delivery of a protein. Therefore, Applicant should not be required to provide an enablement for a separate invention of gene therapy;

2) Applicant's claimed mechanism for delivery of a protein is separate from an invention directed to the use of the protein in a gene therapy method. More specifically, Applicant's claimed invention of a specific mechanism for the delivery of a protein is only one part of a gene therapy invention. In other words, a process to make a product is separate from the use of the product. Applicant believes that this situation can be analogous to Applicant claiming a method of producing time-release high potency Vitamin C tablets, but Applicant is not responsible for any clinical use of the Vitamin C for treatment of diseases. Consequently, Applicant maintains that Applicant should not be required to provide an enablement for the separate invention of gene therapy.

Moreover, Applicant further avoided the therapeutic enabling issue by employing an approach that has been readily accepted, as shown in the primary reference, Hollis et al., which was used by the Examiner in further claim rejections. In the Hollis et al. reference, as well as, other protein expression patents, each uses the same strategy of claiming the expression or production of proteins rather than a specific gene therapy protocol. For example, Hollis et al recites purification of recombinant proteins. Still others adopt similar ways to claim either expression or production of proteins rather than the gene therapy for which the proteins would be used. Applicant has adopted this same approach by claiming the delivery of proteins rather a specific gene therapy protocol.

Applicant is only responsible for enablement of the disclosed method within the scope defined by the claims, not beyond the scope of the claims. As Examiner previously stated on page 4, line 6 of the first Office Action, the present invention is "enabling for delivery of a protein to the blood in vivo". That is precisely the claimed

invention. Now however, the Examiner has withdrawn from this position in this fourth Office Action in order to support his enablement rejection for gene therapy.

However, Applicant has never claimed gene therapy. In fact, in the Background of the Invention, Applicant pointed out that gene therapy comprises many components necessary to obtain a specific gene therapy and each component has many variables. Therefore, it is apparent to the Applicant, the Examiner and those skilled in the art that each component, as well as, the precise gene therapy protocol would be new inventions. However, using the Examiner's unduly expansive interpretation of the claims, the Examiner is in effect denying Applicant's ownership of the claimed protein delivery mechanism just because it can be used in a therapeutic procedure. More specifically, if a precise gene therapy protocol was invented which uses Applicant's claimed protein delivery mechanism, then the Examiner's position denies Applicant's inventive rights to Applicant's claimed invention. It is untenable of the Patent Office to refuse granting Applicant a patent on Applicant's discovered mechanism merely because the discovered mechanism is susceptible of further uses.

The Examiner's rejection is simply unfair and not logical to promoting the useful arts. Applicant maintains that he has complied with the requirements of 35 U.S.C. §112, first paragraph. Applicant's claimed invention has utility for producing and delivering proteins in vivo. The present Specification, page 6, provides a host of utilities for Applicant's claimed invention. More specifically:

> One object of the present invention is to provide a non-tissue specific method that utilizes suitable host cells for synthesis of proteins.
>
> Another object of the present invention is to specifically control the expression and production of proteins in the precursors of the red blood cells.
>
> An additional object is to utilize the non nucleated cell nature of the red blood cells to provide an environment that benefits the stability of the proteins after their production.
>
> Yet another object of the present invention is to bypass the secretion and exocytosis pathways for protein release from the manufacturing site.

Even given these utilities, the Examiner argues that none of them provide "reasons" for in vivo production and delivery of proteins as claimed and requires that "the specification must enable the practice of gene therapy of the broad range of disease set forth in the specification." However as previously cited, Raytheon Co. v. Roper Corp, *ibid*, holds that claims are interpreted in light of the specification does not mean that everything in the specification must be read into the claims.

Moreover, even if a reasonable Examiner would construe that the scope of the claimed invention is for use in gene therapy, Applicants should not be required to enable gene therapy. For example, the fact that a valve is used in an instrument does not mean that a claim using a valve must be accompanied with an enabling disclosure of how to make and use the instrument. All that is required is that the valve be described and enabled.

As previously mentioned, the Examiner initially indicated that the invention was enabling for the delivery of protein in vivo, but now, the Examiner has not provided any reason why the claimed invention is not separately enabled for the delivery of protein in vivo, except that the claimed delivery of protein in vivo is used in gene therapy and gene therapy is not enabled by the specification. Applicant maintains the two are separate in nature and should not be construed as one invention requiring the enablement of the other.

On the other hand, recent advances in gene therapy, as shown by the enclosed Exhibit A articles that show gene therapy has been successful in mice at Autonomous University of Barcelona, Spain; dogs at Washington University and the University of Pennsylvania and an 18 month old child at Great Ormond Street Hospital in the United Kingdom. Based on the literature, gene therapy is a feasible approach for medical treatment of diseases. Therefore, it should be understood that Applicant's claimed method can be one method for delivering protein in vivo in a gene therapy protocol, yet is a separate and distinct invention from gene therapy.

Therefore, Applicant maintains that he has complied with the requirements of 35 U.S.C. §112, first paragraph.

Finally, Applicant points out that if further gene therapies are to occur, then the research necessary to discover the gene therapies must be supported by the investment community and the investment community views patents as an essential requirement for funding further research. It would be patently unjust to require an applicant to delay seeking patent protection on one method of a mechanism of protein delivery until after a specific gene therapy has been discovered and proven.

Accordingly, Applicant respectfully requests withdrawal of the rejection of Claims 1, 2, 6-8, 11, 12 and 14, the remaining pending claims, based upon 35 U.S.C. §112, first paragraph.

It is respectfully submitted that Claims 1, 2, 6-8, 11, 12 and 14, the remaining pending claims, are now in condition for allowance and such action is respectfully submitted. Applicant's Agent respectfully requests direct telephone communication from the Examiner with a view toward any further action deemed necessary to place the application in final condition for allowance.

11/15/2002
Date of Signature

By: _____
Yi Li
Registration No. 44,211
Agent for Applicant
Telephone: (786) 242-9349

Address correspondence to:

CUSPA Technology Law Associates
11820 SW 107 Avenue
Miami, FL 33176

Claims With Changes Noted

Please amend Claims 1 to:

1. (Thrice Amended) A method for producing and delivering protein in vivo comprising the steps of:

(a) inserting into a vector a promoter which is active only in progenitor cells of red blood cells, and a gene encoding a protein which is non-native to red blood cells, wherein said promoter and said gene are operably linked;

(b) collecting an amount of progenitor cells of red blood cells from a mammal;

(c) transfecting said progenitor cells of red blood cells in vitro with said vector containing said promoter and said gene;

(d) introducing the transfected progenitor cells of red blood cells back to said mammal, wherein the transfected progenitor cells of red blood cells produce altered red blood cells containing said protein which is non-native to red blood cells in vivo in said mammal, and wherein said protein which is non-native to red blood cells is contained only in said altered red blood cells, and thereafter said protein which is non-native to red blood cells is released into a bloodstream [blood stream] of said mammal through rupture of said altered red blood cells.